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Maternal Exposure to Occupational Solvents and Childhood Leukemia

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Key words: solvents; maternal occupational exposure; childhood leukemia; acute lymphocytic leukemia; child.

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Abbreviations:

ALL: acute lymphoblastic leukemia

CI: confidence interval

OR: odds ratio

Outline:

Abstract

Introduction

Materials and Methods

Results

Discussion

References

Tables

ABSTRACT

Many organic solvents are considered probable carcinogens. A population-based case-control study was carried out, including 790 incident cases of childhood acute lymphoblastic leukemia and as many healthy controls, matched on age and sex. Maternal occupational exposure to solvents before and during pregnancy was estimated using the expert method, which involves chemists coding each individual s jobs for specific contaminants. Home exposure to solvents was also evaluated. The frequency of exposure to specific agents or mixtures was generally low. Results were generally similar for the period ranging from two years before pregnancy up to birth and for the pregnancy period alone. For the former period, the odds ratio (OR), adjusted for maternal age and sex, for any exposure to all solvents together, was 1.11 (95% confidence interval (CI): 0.88-1.40). Increased risks were observed for specific exposures such as to 1,1,1-trichloroethane (OR)=7.55, 95% CI: 0.92, 61.97), toluene (OR=1.88, 95% CI: 1.01, 3.47), and mineral spirits (OR=1.82, 95% CI: 1.05, 3.14). There were stronger indications of moderately increased risks associated with exposure to alkanes (C5-C17) (OR=1.78, 95% CI: 1.11, 2.86) and mononuclear aromatic hydrocarbons (OR=1.64, 95% CI: 1.12, 2.41). Risk did not increase with increasing exposure, except for alkanes, where a significant trend (p=0.04) was observed. Home exposure was not associated with increased risk. Using an elaborate exposure coding method, this study shows that maternal exposure to solvents in the workplace does not seem to play a major role in childhood leukemia.

INTRODUCTION

Acute lymphoblastic leukemia (ALL) is the most frequent form of cancer in children (National Cancer Institute of Canada 2004). At this time there is only limited knowledge and evidence on environmental or other risk factors contributing to the incidence of ALL. There are some convincing data showing that ALL can arise *in utero* because characteristic chromosome translocations, that generate chimeric fusion genes unique for each patient s leukemic clone, are found at birth (Greaves 2002); therefore, the pregnancy and periconceptional periods are exposure windows of primary interest to study risk factors that could be involved in childhood ALL.

Fetal exposure to chemical agents is likely to come primarily from maternal exposure at work. Among chemical agents with carcinogenic potential and to which a substantial proportion of workers is likely to be exposed, are organic solvents. In a multi-site case-control study of cancer patients in Montréal, Canada, it was estimated that 40 percent of men had been occupationally exposed to at least one solvent over the course of their work careers (Siemiatycki 1991). A solvent is any substance capable of dissolving another substance to form a uniformly dispersed mixture or solution (Stacey 1993). In industrial processes, water, a polar solvent, is often incapable of dissolving a large number of substances and therefore organic liquids are used. The expressions industrial solvents or organic solvents are conventionally applied to these organic liquids (Stacey 1993).

Previous studies assessing parental occupational exposures for ALL have not always evaluated maternal exposures or have done so in studies of small size where a substantial proportion of mothers were homemakers, often leading to few usable results (Colt and Blair 1998). More recent and larger studies have included an assessment of maternal exposures; one reported solvents as an exposure category (Schuz et al. 2000), while another reported results on specific solvents or groups of solvents, but in both studies, exposure assignment seems to have been directly based on parents self-reporting (Shu et al. 1999). Recently, McKinney at al. (2003) used parental self-report and a group of professionals to assign exposure to occupational groups (a mixture of occupations, industries, and groups of agents). Overall, results from previous studies, which reported on solvents and leukemia have not been consistent. We conducted a case-control study of childhood leukemia using the expertise of trained chemists to determine maternal exposure to occupational solvents.

MATERIALS AND METHODS

Case ascertainment

Details of the study have been described elsewhere (Infante-Rivard et al. 2000; Infante-Rivard et al. 2001; Infante-Rivard 2003). Briefly, cases of ALL diagnosed between 1980 and 2000 in the province of Québec were recruited from tertiary care centers designated by governmental policy to hospitalize and treat children with cancer in the province. Tracing cases from these hospitals is equivalent to population-based ascertainment. Between 1980 and 1993 cases aged 0 to 9 years at diagnosis were recruited for study; between 1994 and 2000 case selection included those up to 14 years old at diagnosis. A case was determined to have ALL (International Classification of

Diseases, Ninth Revision [ICD-9] coding 204.0) (WHO 1975) on the basis of a clinical diagnosis by an oncologist or a hematologist. Because cancer care is covered under a universal health plan, we believe that a negligible number of children, if any, were treated outside the province.

Control selection

Population-based controls (one per case) were matched on gender and age at the time of diagnosis (calendar date) and, thus, were concurrently selected. From 1980 to 1993, the population-based controls were chosen from family allowance files. The family allowance is a government stipend awarded to all families with children living legally in Canada. This source of data was the most complete census of children for the study years. According to the expected distribution of cases based on matching criteria, a list of ten potential controls was randomly chosen from the lists. Between 1994 and 2000, we used the provincial universal health insurance files as a source for controls, which is an equivalently complete census of children. It was a better source of data for that time period because family allowances were more often directly deposited in the mother s bank account, which meant that the home address was no longer available in the file. We proceeded the same way to obtain potential controls.

Study participants

Children who were adopted, who lived in foster families, whose families spoke neither French nor English, who were not resident in Canada, or whose parents were both unavailable for interview were excluded. Eight hundred and forty-eight eligible cases were identified and the parents of 790 (93.1 percent) were interviewed; out of 916 eligible controls, 790 parents were interviewed (86.2 percent). The reasons for nonparticipation were confidential telephone number, refusal to participate, or inability to trace the family. The study was approved by each hospital s institutional review board, as well as by the provincial agency regulating access to public databases with nominal information. We requested that the parents return a signed informed consent form for the interview.

Data collection

Soon after the anticipated reception of a letter introducing the general purpose to the study, trained interviewers contacted the parents to schedule an appointment for the interview, which was administered by telephone using structured questionnaires. Questionnaires were reviewed as they came in and feedback was given regularly to interviewers. One questionnaire addressed general risk factors and potential confounders. For the assessment of maternal occupational risk factors, the procedure was as follows: a complete job history was obtained from the mother for the period ranging from age 18 years to the end of pregnancy. This information included the job title, and dates on this job, the type of industry and its name and address. For each job held by the mother from two years prior to pregnancy and up to birth of the index child, a semi-structured questionnaire was used to probe the details of each job; as previously described (Goldberg et al.2001), the information collected included the company s activities, raw materials used, machines used, produced goods, responsibilities for machine maintenance, type of room or building in which the woman worked, activities of workmates, presence of gases, fumes, dusts, biocides, oils, solvents, ionizing and non-ionizing radiation sources, use of area or personnel protective equipment, and a detailed open-ended description of the woman s typical activities at work. In addition, for frequent job titles and/or jobs with a significant potential for occupational exposures (such as nurse, sewing machine operator, hairdresser, waitress, cook, textile dry cleaner, knitting and weaving operator), a specialized questionnaire was also administered which probed more deeply into the specific tasks, the time spent at them, specific exposures related to these tasks, and the environment in which they were conducted.

Exposure Coding

Exposure coding was carried out by a team of chemists and industrial hygienists who have many years of experience in exposure assessment in community-based case-control studies. They first assigned each occupation to standard Canadian industrial titles (at the three-digit level) and job titles (at the seven-digit level) (Statistics Canada 1980, 1992). The next step was to determine if there was or was not exposure to specific solvents or chemical mixtures with solvents (the list is shown in Table 1 and discussed later); the complete list of chemicals that were coded includes over 300 items, but the focus here is on solvents, as these were the chemicals of primary interest of the study. The strategy to code exposures from individual job histories is termed the expert method in the occupational epidemiology literature (Teschke et al. 2002), and has been described earlier (Gérin et al. 1985; Siemiatycki et al. 1987). Briefly, experienced chemists use all the available information provided by the study subject, information accumulated from coding exposures for thousands of jobs held in the same geographical area (albeit for men) (Siemiatycki 1991), and their personal knowledge or consultants knowledge of the industries. Chemists were blind to the case/control status.

Each job held by the mother during the two years before pregnancy and during the pregnancy of the index child was coded separately. For each specific chemical or mixture of chemicals on our list, the chemists indicated the presence of exposure; their degree of confidence that the exposure had actually occurred (possible , probable , definite); the frequency of exposure during a normal workweek (<5 percent, 5-30 percent, or >30 percent of the time, coded respectively 1, 2, and 3); and the level of concentration. A low concentration (coded as 1) was assigned if the subject had been exposed to a concentration slightly above background level in the general environment; a high concentration (coded as 3) was assigned if the subject was exposed to the highest possible level of exposure for this chemical encountered in our study population, such as for example, if the subject was using a solvent herself in an enclosed area with poor ventilation, and a medium concentration (coded as 2) was coded when the situation was intermediate.

The list of agents coded (and shown in Table 1) includes several solvents. Some of these are specific chemicals (e.g., benzene, toluene, etc.), and some are complex mixtures of variable composition (e.g., mineral spirits, gasoline). A detailed definition of each specific agent listed in the table can be found elsewhere (Siemiatycki 1991). Most are well-known agents whose meaning we have not altered from that conventionally understood. All the substances analyzed in this paper can be used as industrial solvents but they may have had other uses in the subjects studied here. For instance, benzene is a well-known industrial solvent but can also be used as a chemical reagent; gasoline is more commonly known as fuel but can be used as a solvent, most notably by garage mechanics since it is readily available to them.

Many of the agents fall into various chemical families, and many mixtures contain chemicals that fall into various chemical families. For seven chemical families, listed in the footnote in Table 1, we regrouped subjects by means of the matrix in Table 1. In this matrix, the inclusion of a specific chemical signifies that it is part of the chemical family, while the inclusion of a mixture signifies that it includes chemicals that are part of that chemical family.

Home exposure to solvents

In the general questionnaire, there were items on hobbies which involved exposure to solvents such as model building, furniture stripping, and types of art work; on activities carried out in and around the home with the potential for similar exposure such as electronic and motor vehicle repair; and finally on painting in the home. For each question, we asked about who carried out the activity, and during what time period specified as one year before pregnancy, during pregnancy and from birth to the reference date.

Statistical analysis

Two periods were defined: the first ranges from two years before pregnancy up to birth, and the second includes only the pregnancy period. We used conditional logistic regression to estimate odds ratios (OR) and 95 percent confidence intervals (CI). Each agent, mixture, and family, was analyzed in a separate model and the analyses were adjusted for maternal age and level of schooling. Results are first presented contrasting any exposure with no exposure. For the exposure period ranging from two years before pregnancy up to birth, we repeated the analysis contrasting any exposure with no exposure but this time taking into account the chemist s confidence factor in coding. In the latter analysis, if the chemist had coded the exposure as possible (as opposed to probable and definite), exposure was assigned to the no exposure category. For the same time window, we also conducted an analysis with three levels of exposure: level 0 (baseline), or no exposure (defined as: none coded or exposure coded with a possible confidence); level 1, or some exposure (exposure resulting in concentration X frequency less than 4), and level 2, or greater exposure (concentration X frequency greater than or equal to 4). Finally, we used a model that includes all specific agents and mixtures. We analyzed residential exposure to solvents in the household as never/ever for each question.

RESULTS

The distribution of socio-demographic characteristics between cases and controls was quite similar (Table 2).

Over 99 percent of mothers in both the case and control group answered their own questionnaire. The proportion of women with gainful employment in both groups was almost equal (Table 3). Control mothers had an average of 1.33 jobs over the study period, whereas case mothers had an average of 1.29 jobs. Thirteen job titles among the fifteen most frequently held were similar between case and control mothers. There were more sewing machine operators and cosmetologists among case mothers than among control mothers.

Most exposure frequencies to specific agents or mixtures in the period spanning from 2 years before pregnancy to birth were low (data not shown). For individual chemicals and mixtures, case mothers were more often exposed than control mothers to 1,1,1-trichloroethane (7/1), toluene (32/19), turpentine (5/3), methyl ethyl ketone (4/0), mineral spirits (45/21), and leaded gasoline (5/3). However, control mothers were more often exposed to methanol (30/20), isopropanol (134/121), chloroform (10/2), diethyl ether (12/7), benzene (8/4), and unleaded gasoline (8/6). With respect to chemicals regrouped under chemical families, except for aliphatic alcohols (cases=168; controls=191), cases were more often found to be exposed than controls (alkanes: 56/32; aliphatic ketones: 23/19; mononuclear aromatic hydrocarbons: 95/63), or the frequency was the same (chlorinated alkanes (22/21) and chlorinated alkenes (12/12). Exposure to the general category of solvents (331/322) was similar in both groups.

In Table 4, we show adjusted odds ratios for exposure to specific chemicals, mixtures, chemical families, and the general solvents category. Differences in the odds ratios between the two periods (two years before pregnancy and up to birth and only during pregnancy) were minor. The same number of women was working in both periods, but a smaller number of jobs were held during the pregnancy period reducing the opportunities for exposure. With respect to the individual agents and the mixtures, increased risks were observed for 1,1,1-trichloroethane, toluene, mineral spirits, and leaded gasoline. There were stronger indications of moderately increased risks associated with alkanes (C5-C17) and mononuclear aromatic hydrocarbons for both period. No risk increase was observed for the general category of solvents.

Results comparing exposed to non-exposed mothers accounting for confidence in the coding are shown in Table 5; odds ratios are quite similar to those reported in Table 4, where confidence level was not considered, except possibly for methylene chloride and chlorinated alkanes where they are higher. Exposure frequencies at the highest level were very low (below 1% for most contaminants), and there was no indication of increased risk with increased level of exposure, except for alkanes where a significant trend (p=0.04) was observed.,

Another analysis was carried out, including in the model all the specific chemicals and mixtures, except those with empty cells, and using the entire target period. Those results show that 1,1,1-trichloroethane (OR=8.16; 95% CI: 0.85, 78.35), toluene (OR=1.94; 95% CI=0.98, 3.84), leaded gasoline (OR=8.16; 95% CI: 0.85, 78.35) and mineral spirits (OR=1.76; 95% CI: 0.97, 3.19) remained associated with increased risks.

Finally, with respect to residential exposure to solvents, we found no increased risk associated with any activity, including those involving the post-natal period (data not shown).

DISCUSSION

The distribution of jobs between case and control mothers was remarkably similar, with a few exceptions, the main one being that there were more sewing machine operators in the case group. This was previously reported for the study subjects included between 1980 and 1993 (Infante-Rivard and Deadman 2003). Despite the fact that prevalence of any exposure to unspecific solvents as a whole was substantial, that to specific agents or mixtures was low and even lower at the highest levels for these agents. For the solvents category, cases and controls had a similar exposure prevalence. Among the specific agents and mixtures to which mothers were exposed prior to or during pregnancy, and that were associated with increased risk of ALL were: 1,1,1-trichloroethane, toluene, mineral spirits, leaded gasoline, and possibly methylene chloride and methyl ethyl ketone. Among the chemical families, there were stronger indications of increased risk for alkanes (C5-C17), and mononuclear aromatic hydrocarbons.

In a recent review on organic solvents and cancer, Lynge et al. (1997) reported that there is some evidence for an increased risk of cancer with toluene, 1,1,1-trichloroethane, and methylene chloride, although none is classified yet as a carcinogen by any regulatory agency. The US National Institute of Occupational Health (1978) issued a bulletin on chloroethanes stating that 1,1,1-trichloroethane should be treated in the workplace with caution because of its structural similarity to other chloroethanes shown to be carcinogenic in animals. Mineral spirits are refined petroleum solvents that include varnish makers and painters naphtha, Stoddard solvent and White spirits (Siemiatycki 1991). Their composition is largely made of saturated hydrocarbons (or alkanes, which in liquid form are C5-C17), but also includes a small proportion of benzene. Although benzene is a recognized leukemogenic agent (IARC 1987), there is little information on the carcinogenicity of mineral spirits as such; a Swedish study reported an increased risk of acute leukemia among painters (Lindquist et al. 1987), but painters may be exposed to a greater extent to other solvents such as toluene and xylene. Leaded gasoline, another mixture that showed indications of increasing risk, is a mixture of hydrocarbons used as fuel for automobiles; it also contains benzene and toluene. A fairly consistent link between fathers with occupations in motor vehicle-related occupations and childhood leukemia has been reported (Colt and Blair 1998); however, such occupations involve exposure to a variety of chemicals including polycyclic aromatic hydrocarbons such as benzo[a]pyrene, which is considered a probable or suspected carcinogenic agent by regulating agencies (IARC 1983).

Results from studies on maternal occupational exposures and childhood ALL published between 1980 and 1997 (Hemminki et al.1981; Gold et al. 1982; Van Steensel-Moll et al. 1985; McKinney et al. 1987; Lowengart et al. 1987; Shu et al. 1988; Magnani et al. 1990; Olsen et al. 1991; Feingold et al. 1992) have been reviewed before (Colt and Blair 1998). In all these studies, with the exception of that by Feingold et al. (1992), exposure was defined as having an occupation or belonging to an industry, or occasionally, exposure to a specific agent was reported, as determined by maternal reporting. This strategy was also used in a more recent study from Germany (Schuz et al. 2000), not included in the review. On the other hand, Feingold et al. (1982) used a general job-exposure matrix to determine exposure to a list of specific agents; unfortunately, this study was very small (approximately 60 cases of ALL and 60 controls), and results were inconclusive. In a more recent and large study from the US (Shu et al. 1999), mothers reported specific exposures as well as the approximate length of time spent being exposed to a particular agent. No additional strategy to code exposure involving chemists or similar experts is explicitly described so it is assumed that the self-reported reported exposures were used as such. Finally, in another recently published and large study, this time from the UK (McKinney et al. 2003), occupations and industries were coded according to standard classifications; in addition, a panel of experts, including an hygienist, created 31 occupational groups that were said to be homogeneous for specific exposures. The occupational groups used in the analysis include job titles (e.g., leather workers), sectors of activity (e.g., agriculture) and agents such as solvents and hydrocarbons (skin/epidermal or inhaled particulate). The method to create the groups is not detailed in the paper. Because of the different ways to classify exposures and the multiple classifications used (even for job titles or industries, each study using their respective national classification), results are difficult to compare. However, in the three more recent studies (Schuz et al. 2000; Shu et al. 1999; McKinney et al. 2003), an explicit solvents category was used, and results are as follows: Schuz et al. (2000) report an odds ratio of 1.2 (95 percent CI: 0.9, 1.7) for exposure to solvents during periconception and a similar result during pregnancy. Shu et al. (1999) report an OR of 1.8 (95 percent CI: 1.3, 2.5) for exposure to possible organic solvents during preconception (2 years previous to conception) and a similar result during pregnancy. Finally, in the McKinney et al. study (2003), the OR associated with exposure to solvents at periconception was 1.0 (95 percent CI: 0.66, 1.51); however, exposure to dermal hydrocarbons had an OR of 2.16 (95 percent CI: 1.16, 4.02).

The present study uses the most detailed and elaborate exposure assessment method in comparison with previous ones. The expert method used here has been found to have good validity (Fritschi et al. 2003). Its steps have been clearly detailed (Siemiatycki 1991), and results using this method to uncover carcinogens in community-based case-control studies have been abundantly published (Parent et al. 2000; Aronson et al. 1996). In this study, all specific agents associated with increased risk have also been associated with increased risks of cancer in previous studies. Whereas results for some specific agents or families were indicative of increased risk, this was not as clear for the general category solvents . The families of alkanes (C5-C17) and mononuclear aromatic hydrocarbons are ones which many previous studies have tried to capture by using the hydrocarbon-related occupations (Van Steensel-Moll et al. 1985; Lowengart et al. 1987; Shu et al. 1988; Olsen et al. 1991; Shu et al. 1999; McKinney et al. 2003). The result by McKinney et al. (2003) showing a substantial increase in risk associated with periconception dermal exposure to hydrocarbons is coherent with our own. Overall, our results on alkanes and mononuclear aromatic hydrocarbons are coherent with and reinforce previous results. However, with the exception of alkanes, it was disconcerting to find no indication of an exposure-response relationship, an observation also reported by Shu et al. (1999).

A study reported results on home exposure to solvents and childhood ALL (Freedman et al. 2001). Only artwork at a frequency of more than 4 times a month was associated with an increased risk of ALL. We did not measure frequency of exposure for home solvents, but none of the odds ratios in our study were indicative of any increase in risk for the ever-exposed category.

In comparison with previous studies on parental occupational exposures and childhood ALL, this is the third largest in terms of number of cases. Nevertheless, power is still an issue. With respect to potential biases often affecting case-control studies, in this study, selection bias was unlikely: participation rates for cases and especially for controls were markedly higher (by approximately 20 percent) than in any of the other large studies cited. However, although the exposure assignment method used in this study seems more refined than in previous studies, it is safe to say that nondifferential misclassification of exposures affected the results and reduced our ability to uncover significant findings.

In conclusion, this study used an exposure assignment method that is among the best available for community-based case-control studies of cancer. The results gave more specific indications than previous studies and point to increase in ALL risk associated with maternal exposure to occupational alkanes and mononuclear aromatic hydrocarbons. Nevertheless, they are still somewhat uncertain. From a public health point of view it was reassuring to observe that, as in all previous studies, maternal exposures were most often rare and occurred at low levels; this of course makes the task of uncovering effects more difficult. However, this fact should not deter us from a continued search in this direction because prenatal exposure to carcinogens as risk factors for childhood leukemia makes biological sense, and even low levels during this period could be damaging. We are thus challenged to develop more sensitive methods to ascertain parental occupational exposures. Adding a genetic susceptibility perspective could also enhance our ability to uncover the susceptible dyads (mother and child).

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Table 1. Matrix of specific chemicals, complex mixtures of chemicals and chemical families used in the analysis.

	ID[b]	Chemical families[a] 1	2	3	4	5	6	7
SPECIFIC CHEMICALS								
Methanol	232		xx[c]					
Ethanol	233		xx					
Isopropanol	234		xx					
Ethyleneglycol	235		xx					
Carbon tetrachloride	237			xx				
Chloroform	238			xx				
Methylene chloride	239			xx				
1,1,1-trichloroethane	240			xx				
Trichloroethylene	242				xx			
Perchloroethylene	243				xx			
Ethylene dichloride	300				xx			
Acetone	248					xx		
Methyl ethyl ketone	304					xx		
Benzene	252						xx	
Toluene	253						xx	
Xylene	254						xx	
Ethyl acetate	302							xx
Diethylether	250							
Turpentine	280							
Carbon disulfide	266							
Butyl cellosolve	306							
MIXTURES								
Mineral spirits post-1970	202	x[d]					x	
Mineral spirits pre-1970	203	x					x	
Leaded gasoline	191	x					x	
Unleaded gasoline	299	x					x	
Aviation gasoline	190	x					x	
Kerosene	195	x					x	

[a] 1= alkanes (C5-C17); 2= aliphatic alcohols; 3= chlorinated alkanes; 4=chlorinated alkenes; 5= aliphatic ketones; 6= mononuclear aromatic hydrocarbons; 7= aliphatic esters

[b] These ID codes were used in reference #3 to catalogue and define the various substances, and they can thus be used to easily find additional information on these chemicals in that reference.

[C] This signifies that the agent listed on the vertical axis is a member of the chemical family listed on the horizontal axis.

[d] This signifies that the agent listed on the vertical axis contains components that are members of the chemical family listed on the horizontal axis.

Table 2. Demographic characteristics (number and percent) of ALL cases and controls

	Cases (n=790) nb (%)	Population Controls (n=790) nb (%)
Mother s education		
None or primary school	34 (4.3)	25 (3.2)
Secondary school	437 (55.3)	436(55.2)
College or university	319 (40.4)	328 (41.6)
Mother s age at child s birth		
< 35	721 (91.3)	743 (94.0)
35	69 (8.7)	47 (6.0)
Family income at diagnosis		
40,000	312 (39.9)	309 (40.2)
10,000-39,000	427 (54.7)	422 (54.9)
<10,000	42 (5.4)	38 (4.9)

Table 3. Distribution of job titles among mothers of ALL cases and population controls during the period ranging from two years before pregnancy up to birth of the index child

	Cases	Controls
Not working	178 (22.5%)	173 (21.9%)
Number working	612	617
Nb of jobs held	792 (average: 1.29)	820 (average: 1.33)
Job titles by order of frequency		
	Secretary	Secretary
	Clerk (general office)	Clerk (general office)
	Sewing machine operator	Waitress
	Waitress	Nurse (general duty)
	Cashier (clerical)	Cashier (clerical)
	Nurse (general duty)	Teller
	Cosmetologist	Sales clerk
	Sales clerk	Elementary school teacher
	Teller	Sewing machine operator
	Elementary school teacher	Cashier (customer service)
	Baby sitter	Cosmetologist
	Receptionist	Receptionist
	Computer operator	Baby sitter
	Accountant clerk	Accountant clerk
	Nurse s aide	Counterwoman (cafeteria)

Table 4. Adjusted[a] odds ratio (OR) for maternal exposure to solvents

	2 y prior to pregnancy up to birth		during pregnancy	
	OR[b] (95% CI)	RDP[c]	OR (95% CI)	RDP
Specific chemicals				
Methanol	0.77 (0.41, 1.47)	17/22	0.78 (0.39, 1.55)	15/19
Ethanol	1.22 (0.66, 2.25)	23/19	1.06 (0.55, 2.03)	19/18
Isopropanol	0.96 (0.71, 1.29)	85/89	0.95 (0.69, 1.31)	73/78
Chloroform	0.25 (0.05, 1.17)	2/8	0.25 (0.05, 1.17)	2/8
Methylene chloride	1.34 (0.54, 3.34)	11/8	1.25 (0.46, 3.35)	9/7
1,1,1-trichloroethane	7.55 (0.92, 61.97)	7/1	4.07 (0.45, 36.7)	4/1
Perchloroethylene	0.96 (0.41, 2.25)	11/11	0.84 (0.30, 2.34)	7/8
Acetone	1.05 (0.53, 2.08)	17/16	1.13 (0.52, 2.44)	14/12
Methyl Ethyl Ketone	-	4/0	-	4/0
Benzene	0.82 (0.22, 3.06)	4/5	1.39 (0.31, 6.25)	4/3
Toluene	1.88 (1.01, 3.47)	29/16	2.25 (1.02, 4.95)	20/9
Diethyl ether	0.50 (0.17, 1.48)	5/15	0.63 (0.20, 1.93)	5/8
Turpentine	1.76 (0.42, 7.42)	5/3	1.76 (0.42, 7.42)	5/3
Mixtures				
Mineral spirits post-1970	1.82 (1.05, 3.14)	37/20	1.66 (0.86, 3.22)	24/14
Minerals spirits pre-1970	-	5/0	-	4/0
Leaded gasoline	5.09 (0.59, 43.65)	5/1	4.14 (0.46, 37.16)	4/1
Unleaded gasoline	0.90 (0.30, 2.71)	6/7	0.83 (0.22, 3.10)	4/5
Chemical families [d]				
Alkanes (C5-C17)	1.78 (1.11, 2.86)	48/27	1.72 (0.98, 3.03)	33/19
Aliphatic alcohols	0.90 (0.68, 1.18)	97/108	0.89 (0.66, 1.20)	84/95
Chlorinated alkanes	1.33 (0.68, 2.61)	20/15	1.05 (0.50, 2.19)	15/14
Chlorinated alkenes	0.97 (0.43, 2.17)	12/12	0.86 (0.33, 2.25)	8/9
Aliphatic ketones	1.30 (0.68, 2.50)	21/16	1.46 (0.70, 3.03)	18/12
MAH [e]	1.64 (1.12, 2.41)	70/43	1.68 (1.06, 2.67)	49/29
Solvents [f]	1.09 (0.87, 1.38)	154/141	1.00 (0.78, 1.28)	125/125

[a] Adjusted for maternal age and level of schooling; specific chemicals or mixtures with less than 4 exposed mothers are not shown in the table.
[b] Odds ratio (and 95% confidence interval) for any exposure: Baseline is no exposure
[c] Ratio of discordant pairs
[d] Chemical families regroup specific chemicals that belong to a family and mixtures that have components belonging to it
[e] Mononuclear aromatic hydrocarbons
[f] Includes all specific chemicals and mixtures in the table

Table 5. Adjusted odds ratios[a] and 95% confidence intervals for levels of maternal exposure to solvents during the two years prior to pregnancy up to birth.

	Probable/definite *vs*. possible/no exposure		Level 1[b] *vs*. possible/no exposure		Level 2[c] *vs*. possible/no exposure	
Specific chemicals						
Methanol	0.81	0.43, 1.55	0.81	0.38, 1.70	0.82	0.25, 2.77
Ethanol	1.11	0.59, 2.08	1.44	0.61, 3.39	0.81	0.32, 2.07
Isopropanol	0.97	0.72, 1.31	0.92	0.65, 1.32	1.09	0.65, 1.84
Chloroform	0.16	0.02, 1.36	0.30	0.03, 2.90	-	
Methylene chloride	3.22	0.88, 11.73	4.68	0.55, 40.20	2.49	0.48, 12.81
Perchloroethylene	0.87	0.35, 2.18	0.95	0.35, 2.55	0.55	0.05, 6.34
Acetone	1.11	0.54, 2.29	0.95	0.39, 2.28	1.55	0.43, 5.51
Benzene	0.77	0.17, 3.48	-		1.47	0.25, 8.85
Toluene	1.98	1.06, 3.72	3.19	1.43, 7.12	0.68	0.18, 22.05
Diethyl ether	0.63	0.20, 1.94	0.67	0.19, 2.41	0.51	0.04, 5.59
Turpentine	1.76	0.42, 7.42	1.64	0.27, 9.92	2.00	0.18, 22.05
Mixtures						
Mineral spirits post-1970	1.74	0.99, 3.06	1.60	0.86, 2.98	2.50	0.66, 9.46
Chemical families [d]						
Alkanes (C5-C17)*	1.78	1.09, 2.91	1.56	0.91, 2.67	3.39	0.94, 12.21
Aliphatic alcohols	0.91	0.69, 1.20	0.89	0.64, 1.23	0.95	0.60, 1.51
Chlorinated alkanes	2.00	0.90, 4.47	2.18	0.67, 7.10	1.86	0.62, 5.57
Chlorinated alkenes	0.89	0.37, 2.11	1.07	0.41, 2.80	0.35	0.03, 3.53
Aliphatic ketones	1.40	0.71, 2.77	1.24	0.54, 2.84	1.80	0.52, 6.17
MAH [e]	1.67	1.13, 2.48	1.82	1.15, 2.87	1.32	0.62, 2.80
Solvents [f]	1.11	0.88, 1.40	1.11	0.85, 1.46	1.11	0.75, 1.63

[a] Adjusted for maternal age and level of schooling
[b] Defined as concentration x frequency <4: baseline is possible or no exposure
[c] Defined as concentration x frequency 4
[d] Chemical families regroup specific chemicals that belong to a family and mixtures that have components belonging to it
[e] Mononuclear aromatic hydrocarbons
[f] Includes all specific chemicals and mixtures in the table
* p-value for trend=0.04